Accelerating Medicines Partnership: Alzheimer's Disease

The National Institutes of Health (NIH), 10 biopharmaceutical companies, and several non-profit organizations have designed an unprecedented new partnership. Managed through the Foundation for the NIH (FNIH), the Accelerating Medicines Partnership (AMP) brings high-level government, industry, and non-profit organization partners together to identify and validate the most promising biological targets of disease for new diagnostic and drug development. The partners have designed a bold milestone-driven research plan to tackle this challenge for **Alzheimer's disease**, as well as for type 2 diabetes and the autoimmune disorders of rheumatoid arthritis and systemic lupus erythematosus (lupus). Importantly, the AMP data and analyses will be made publicly available to the broad biomedical community. This fact sheet addresses the AMP research plan for Alzheimer's disease.

Alzheimer's Disease

Dementia, of which Alzheimer's disease is the most common form, is estimated to affect 36 million people worldwide. This number is expected to rise to 115 million by 2050 unless an effective therapeutic is developed. The financial toll of dementia is already staggering: in the U.S. alone, the costs of caring for people over 70 with dementia were estimated to be as high as $215 billion in 2010. AD is characterized by the presence of two signature brain lesions: plaque deposits between nerve cells composed of fragments of the protein, amyloid beta (Aβ), and neurofibrillary tangles (NFT) composed of aggregated tau proteins in the interior of cells.

AMP Alzheimer's Disease
The Partners

Government
- NIH

Industry
- AbbVie
- Biogen Idec
- GlaxoSmithKline
- Lilly

Non-Profit Organizations
- Alzheimer's Association
- Foundation for the NIH
- Geoffrey Beene Foundation
- USAgainstAlzheimer's

Need for New Therapies

The evidence linking Aβ plaque accumulation as the cause of AD has resulted in the development of therapies by many biopharmaceutical companies. However, none to date has demonstrated clinical efficacy in patient trials. These failures may reflect problems with specific molecules and/or trial design rather than the underlying hypothesis. There is a pressing need for improved tools to support target validation in patients prior to Phase III clinical trials and to identify new targets that provide alternative approaches to targeting the disease process. Additionally, it is critical to identify reliable biomarkers that are predictive of clinical response to therapeutic intervention.

AMP Approach

Human genetic studies have been critical in developing our understanding of AD and have recently provided new targets for drug development, such as brain inflammation, immune function, and cellular trafficking, in addition to more traditional targets such as beta-amyloid. The lack of data from clinical trials in humans to support target validation requires new approaches. Capitalizing on the

collective expertise and resources from public-private partnerships may address this gap. This

proposal seeks to a) identify markers of the disease (biomarkers) that can predict clinical outcomes by incorporating selected biomarkers into four NIH-funded clinical trials, which include industry support, designed to delay or prevent disease onset; b) conduct a large-scale analysis of human AD patient brain tissue samples to validate biological targets previously shown to play key roles in disease progression and, more significantly, to increase our understanding of the molecular pathways involved in the disease to identify new potential therapeutic targets. While past studies have demonstrated the promise of several AD biomarkers, this proposal aims to establish an expanded set of biomarkers that can be embedded in therapeutic trials as well as identify new biological targets for drug development.

Governance

The AD arm of the AMP initiative will be managed by an AD steering committee (SC), comprising representatives from NIH, FNIH, the Food and Drug Administration (FDA), and participating companies and patient advocacy organizations. After AMP research grant awards are made, investigators carrying out the research will be added to the disease SCs. The SC will operate under the direction of the overall AMP Executive Committee (EC), which includes representatives from NIH, participating industry partners, FDA, and patient advocacy organizations. The SC is responsible for reporting project plans and milestones to the EC for review and approval, and will meet on a regular to assess project progress.

Timeline and Deliverables

This will be a five-year endeavor, beginning in early 2014. For the project on biomarkers, the tau imaging and EEG data will be released in year two, as baseline data become available. Final data from the randomized, blinded trials will be added after the end of the five year studies, and will include both the imaging data and data from blood and spinal fluid biomarker studies. For the network analysis project, each individual project will generate several network models of late onset AD (LOAD) and will identify key drivers of disease pathogenesis by the end of year three. Years four and five will be largely dedicated to validating the novel targets and refining the network models of LOAD, including screening novel compounds or drugs already in use for other conditions that possess the ability to modulate the likely targets.

Budget: 5 years ($129.5 Million Total Project Funding)

($Millions)	Total Project	Total NIH	Total Industry
Alzheimer's Disease	129.5	67.6	61.9